THE AMERICAN
JOURNAL OF PHARMACY

MARCH, 1899.

THE ASSAY OF BELLADONNA LEAVES AND SOME OF ITS PREPARATIONS.[1]

By Frank X. Moerk.

The results recorded in this paper were obtained in an investigation made for the J. Ellwood Lee Company, of Conshohocken, Pa., to determine the alkaloidal strength of belladonna plaster, U.S.P., 1890. After a survey of the work done by others in a similar direction, it was decided to purchase several pounds of the different commercial varieties of belladonna leaves, have these examined by a pharmacognocist for adulterations or admixture, then grind and use them for assay and manufacturing purposes. Accordingly, the three following commercial varieties were purchased: (1) English cultivated, Allen's; (2) German cultivated; and (3) German wild.

These were submitted to Professor Henry Kraemer for examination; his report, addressed to me, is as follows:

"I have carefully examined the three lots of belladonna leaves you sent me, and find them to be as follows:

"(1) The *English drug* is made up mostly of belladonna leaves with a few stems. Numerous mature and immature flowers are present, indicating that the drug was collected in early summer. The leaves are of a uniform green color, and the drug has a heavy narcotic odor.

"(2) The *German cultivated drug* consists chiefly of leaves with

[1] Read at the Pharmaceutical Meeting of the Philadelphia College of Pharmacy, February 21, 1899.

a few stems and some flowers and some rather immature fruits. The drug appears to have been collected some time during the middle of summer. Most of the leaves are of a green color upon both surfaces; the upper surface of the others is of a brownish color, the lower being greenish.

"(3) The *German Wild Drug* is made up of leaves, numerous stems, and shows some indications of the entire plant (when a year or two old) having been collected. There are numerous mature fruits, which indicate that this specimen was collected later in the season than the other two specimens. The leaves vary in color from an etiolated, yellowish green to brownish-black. The latter color indicates that little or no care was exercised in drying the drug."

The samples were then ground and used in the following work:

ASSAY OF THE LEAVES.

The method of C. C. Keller was looked upon favorably, and selected for the determination of the alkaloids. The writer regrets that he was not able to see the original publication in the *Schweiz. Wochenschrift für Pharm. u. Chemie*, and therefore had to content himself with the following abstract from the *Proc. Am. Pharm. Assoc.*, 1895, pp. 536 and 541:

Belladonna leaves, No. 80 powder (dried over CaO or H_2SO_4)	25	grammes.	
Ether	100	"	
Chloroform	25	"	
Ammonia water, 10 per cent.	10	"	
Water	40	"	
Pour off	100	"	(= 20 grammes drug).

Place the drug in a bottle of 250 c.c. capacity, add the ether and chloroform, agitate for ten minutes, then add the ammonia water and agitate vigorously; continue maceration for one-half hour, add the water and agitate thoroughly to gather the drug in lumps so that the solution can be poured off clear. In case 100 grammes cannot be obtained at first, pour off as much as possible, and by gentle motion of the bottle, held in a horizontal position and allowing it to rest for a short time, the balance may be obtained. The solution is transferred to a separatory funnel and agitated with diluted hydrochloric acid (0·5 to 1 per cent.) in portions of 25, 15 and 10 c.c. respectively. These acid solutions are then placed in a clean separatory funnel, made alkaline with ammonia and treated

immediately with successive portions of 50, 30 and 20 grammes solvent (= 3 parts chloroform and 2 parts ether by weight). The combined ethereal extractions are set aside for a short time, and then passed through a small filter moistened with ether into a tared flask of 150 to 200 c.c. capacity, and the solvent distilled off. The residue is treated with 2 or 3 small portions of ether, the latter removed by heating the flask in a water-bath; the vapors of ether are finally removed from the flask by means of a current of air from a bellows, and the flask and contents heated in the water-bath for periods of fifteen minutes each, and weighed in the intervals until constant weight is obtained. The alkaloids are dissolved in 5 to 10 c.c. of neutral, absolute alcohol, water added to the beginning of a turbidity and the alkaloids titrated with $\frac{n}{10}$ or $\frac{n}{20}$ hydrochloric acid, using hæmatoxylin as indicator (3 drops of a 1 per cent. alcoholic solution).

As the result of some preliminary assays, several modifications of this process were made: (1) Moisture was determined in a separate portion of 2 grammes at 100° C., and the powdered leaves, without previous drying over lime or sulphuric acid, used in the assay. The reasons for this were that the maximum quantity of moisture present in 20 grammes leaves was about 2 grammes, and this was not considered to be sufficient to interfere with the penetration of the drug by the 125 grammes solvent used; the drying of a portion of the drug at the generally accepted temperature of 100° C. insured figures which could afterwards be utilized in calculating the alkaloid for a perfectly dry drug or for a drug containing a different per cent. of moisture. (2) The determination of alkaloids in the U.S.P. plaster made it likely that sulphuric acid would be preferable to hydrochloric acid, because of the presence of lead salts in the plaster, in removing the alkaloids from the ether-chloroform solution, hence, a diluted sulphuric acid (2 c.c. H_2SO_4, diluted to 500 c.c.) was used. (3) It was found impossible to obtain 100 grammes of the ether-chloroform alkaloidal solution, so that 20 grammes drug were used instead of 25 grammes, with the quantity of solvent unchanged. (4) The extraction with diluted sulphuric acid and the ether-chloroform extraction of the acid solution were made in 4 portions of 25, 15, 10 and 5 c.c. each, the last portion being used to rinse the vessels which had contained the other

portions. A fifth portion of 20 c.c. ether-chloroform was used in a number of assays to determine if the alkaloids were perfectly extracted by the preceding four portions of solvent, but in no case did the residue obtained cause an alkaline reaction with the indicator.

The assay of the leaves therefore was conducted as follows:

Moisture determined in a separate portion of 2 grammes at 100° C.

Assay Proper.—Twenty grammes of the powdered leaves were placed in a glass-stoppered bottle of 250 c.c. capacity, tared, 100 grammes ether and 25 grammes chloroform added; after several minutes' agitation 10 c.c. ammonia water (10 per cent.) were added, and the mixture frequently agitated during one to two hours; after adding 4.0 c.c. H_2O agitate thoroughly for several minutes; set aside for ten minutes, and pour off as much as possible of the ether-chloroform solution into a clean, dry flask of about 150 c.c. capacity. Weigh this flask with contents, and after standing about one-half hour (to allow any drug and aqueous solution which may be carried over, to separate), pour into a separating funnel as much as possible of the clear ether-chloroform solution and weigh the flask with its residual contents. The difference between the two weights gives the weight of the solution transferred, and represents a certain weight of the leaves, the exact amount of the latter being calculated by the proportion:

125 gm., wt. of solvent used : 20 gm. : : wt. of transferred solution : x.

The ether-chloroform solution is extracted with four portions of acidulated water (2 c.c. H_2SO_4 to make 500 c.c.) of 25, 15, 10 and 5 c.c. respectively; the first three portions are collected in one beaker, while the last one is kept separately. After cleaning the separatory funnel the contents of the beaker are returned and the last portion of 5 c.c. acidulated water used to rinse this, and also returned to the separatory funnel; 5 c.c. water are then used to complete the rinsing of the beaker and added to the acid solutions. The acid solution is next agitated with 25 c.c. ether-chloroform (2 parts ether and 3 parts chloroform by weight), 8 c.c. ammonia water (10 per cent.) added and again thoroughly agitated; after separation the ether-chloroform is run into a smaller separator and extraction repeated with 15, 10 and 5 c.c. ether-chloroform; while this last portion is separating the first three portions are filtered through a small filter, wetted with the solvent mixture, into an Erlenmeyer flask of

120 c.c. capacity; the smaller separator and filter are then washed with the last ether-chloroform extraction and later by the use of 5 c.c. of the mixed solvent; finally, wash the stem of the separator and funnel and the filter with about 5 c.c. more of the solvent applied in portions. Distil off the solvent and warm on the water-bath until the odor of chloroform has disappeared; dissolve in 5 c.c. ether, evaporate this, redissolve in 5 c.c. ether and warm until the odor of ether has disappeared. Now dissolve in 8 c.c. neutral alcohol, dilute with 30 c.c. water, add 3 drops hæmatoxylin solution and titrate with standardized HCl to a pure yellow solution. The hydrochloric acid used in all of this work was standardized with fused sodium carbonate and 1 c c. was found the equivalent of 0·02104 grammes mydriatic alkaloids.

EXTRACTUM BELLADONNÆ FOLIORUM ALCOHOLICUM.

While these assays were made the preparation of the extracts from 500 grammes of the leaves was progressing. The powder required for this not being as fine as needed for the assays, moisture determinations of each lot were also made. The Pharmacopœia directions as to the strength of the menstruum were followed, but it was found that the quantity prescribed did not, by appearances, thoroughly extract the drug, hence a quantity about double that ordered was used, and still the percolate was distinctly colored. Authority for this is found in the pharmacopœial directions to continue percolation until a specified quantity of percolate is obtained or the belladonna leaves are exhausted.

The evaporation of the percolate at a temperature not exceeding 50° C., to obtain an extract of *pillular* consistence was a very tedious operation, requiring several weeks' time. Using a weighed evaporating dish and glass rod the yield of extract was readily calculated; as soon as the extract was obtained of a *firm pillular* consistence it was weighed, thoroughly mixed and the several portions needed for moisture determination for assays and for the plaster weighed off without loss of time, and the preparation of the plaster proceeded with.

ASSAY OF THE EXTRACT.

Moisture by drying about 2 grammes at 100° C.

Alkaloidal Assay.—About 5 grammes of the extract were weighed into a beaker and disintegrated by stirring with small portions of a

mixture consisting of 10 c.c. water and 10 c.c. water of ammonia (10 per cent.); the extract mixture was put into a glass-stoppered bottle of 250 c c. capacity, and the beaker rinsed with the remainder of the diluted ammonia water used in portions. Into this bottle were then weighed 60 grammes ether and 15 grammes chloroform, the mixture agitated continuously for ten minutes, and set aside for ten minutes, when the ether-chloroform solution was poured off as completely as possible into a clean, dry flask, weighed and set aside for one-half hour. As much as possible of the ether-chloroform solution was then poured into the separatory funnel, the flask and residual contents weighed (to ascertain the weight of the transferred solution) and the assay proceeded with, as described under the assay of the leaves. The quantity of extract used for the completion of the assay was calculated by the following proportion:

$$75 \text{ gm., wt. of solvent used} : \text{wt. of extract started with} :: \text{wt. of transferred portion} : x.$$

In the assay of the extract from the English cultivated leaves it was found that the first portion of 25 c.c. of acidulated water did not cause an acid reaction, so that 40 c.c. were used in the first portion, followed afterwards by three portions of 5 c.c. each.

EMPLASTRUM BELLADONNÆ, U.S.P., 1890.

As stated before, as soon as the extract of belladonna was obtained of the proper consistency it was weighed, mixed and portions weighed off for the various determinations and for the making of the plaster. Forty grammes each of resin plaster and soap plaster (purchased from a manufacturing house) were melted in a weighed evaporating dish placed on a water-bath and 20 grammes of the extract, weighed on a watch crystal, incorporated by heating on the water bath whilst constantly stirring; unnecessary heating was avoided, but still a loss of about 1 per cent. was noticed in each case; by weighing the contents of the dish before adding the extract a loss of 0·3 to 0·4 grammes was noticed, so that the greater portion of the loss is due to the moisture in the extract used. *In the Pharmacopœia this loss in making Belladonna Plaster has not been recognized.*

Assay of the Plaster.—After several unsuccessful trials of what seemed possible methods, the following was decided upon and found to give conforming results. It depends upon the decomposition of the soap and of the lead salts by sulphuric acid, and from calcula-

tions made 1 c.c. sulphuric acid, U.S.P., is a little more than needed to decompose 10 grammes of the official plaster.

Ten grammes of the belladonna plaster were weighed into a beaker and covered with a mixture of 1 c.c. sulphuric acid and 15 c.c. of water; the plaster is disintegrated by stirring and pressing against the side of the beaker, but is slow, as no heating is allowable saving the heat of the hand; if heating over a burner is resorted to the lead sulphate and fat acids separate in pulverulent form, and are then more difficult to manipulate. The end of the operation is assured when the stirring rod no longer discloses any hard lumps in the putty-like mass produced, if manipulated as described. The acid solution is filtered through a small filter into a separatory funnel and the mass worked with the glass rod so that as much of the solution as possible is separated and removed to the filter. The mass in the beaker is then thoroughly mixed up with two portions of 10 c.c. each of the acidulated water (2 c.c. H_2SO_4 to make 500 c.c.), followed afterwards by three portions of 5 c.c. each, allowing to settle and working up the mass so as to get as much as possible of each portion upon the filter before adding the next portion. After all these portions have run through the filter, wash the latter with a few c.c. of the acidulated water, then add to the contents of the separatory funnel 25 c.c. of the ether-chloroform mixture, 10 c.c. of ammonia water (10 per cent.) and proceed as under the assay of the leaves.

EMULSIFICATION IN ALKALOIDAL EXTRACTIONS.

While emulsification in assays of belladonna leaves and extracts by the described processes were occasionally met with, the assay of belladonna plaster as just described was effectually blocked by the formation of a persistent emulsion. In the case of the leaves and extracts the relatively large proportion of the clear mixed-solvent with the smaller emulsified portion was run into the smaller separator and then generally separated on standing a short time; the aqueous solution thus transferred to the smaller separator was freed from alkaloid by agitation with the portions of solvent used to rinse the separator; in the subsequent filtration care was taken to prevent the aqueous solution passing on to the filter. This manipulation did not avail in the assay of the plaster, and it therefore became necessary to find some expedient which would bring about the separation of the solvent.

It is this particular drawback—the emulsification of the alkaline solution when agitated with the alkaloidal solvent—that has done more than any other single factor to prevent alkaloidal assaying from being more generally applied; it has also given rise in certain assay processes to the direction "to mix the alkaline solution and alkaloidal solvent by a rotary motion, or by gentle agitation," as distinguished from shaking "to prevent emulsification." Such directions may be suitable for extracting alkaloids which are practically insoluble in the alkaline solution, and where one can see the alkaloid dissolving in the solvent, but I cannot believe that total extraction results in case the alkaloid remains soluble in the alkaline solution, as is the case with the belladonna alkaloids. This same view has been expressed by Dr. E. R. Squibb, in a recent article on the assay of ipecac, AM. JOUR. PHARM., 1899, p. 11.

After numerous failures it was found that the addition of a small quantity of stearic acid was effectual in separating the emulsified alkaloidal solvent, and that it could be used after emulsification had taken place, or by adding it before agitating the alkaline solution with the solvent, it would prevent serious emulsification. (Other fat acids while not tried, will very likely produce the same result.) A small quantity, weighing 10 to 15 milligrammes, or even less in many cases, is sufficient, and is best added in several small fragments; if these be shaken vigorously with an emulsified mixture, and then allowed to stand for a few minutes, separation will begin, or can be made to begin by a *twirling* motion imparted to the stem of the separator; it may not be possible to obtain the entire quantity of the solvent at once, but by running off the clear portion to the smaller separator, a portion again of the remaining emulsion will respond to this same coaxing twirling motion, and can be transferred to the previously removed portion, and the operation repeated until only about 1 c.c. emulsion remains. In this way it was found possible to complete, in about two hours, the several extractions in the assay of a plaster, the first extraction of which had remained emulsified for two days. It may happen that a little more stearic acid is needed after the first extraction.

This same separation may be effected by fusing a little stearic acid on the end of a piece of iron wire and stirring the emulsified portion with this, running off the clear solution and repeating the operation; this method, however, involves the taking up of more stearic acid by the solvent.

The question suggested itself: "To what extent does the stearic acid interfere with the accuracy of the assay?" The following experiments answer this question:

(1) 0·100 gramme stearic acid (a quantity far in excess of that actually used in the assays) was dissolved in 10 c.c. alcohol, 1 c.c. of a diluted ammonia water, 30 c.c. water, and 3 drops hæmatoxylin indicator added, required 0·75 c.c. HCl.

(2) In a similar experiment, omitting the stearic acid 0·75 c.c. HCl were needed.

(3) 0·100 gramme stearic acid dissolved in 10 c.c. alcohol, 0·5 c.c. of a more dilute ammonia water, 30 c.c. water, and 3 drops indicator added, required 0·2 c.c. HCl.

(4) A similar experiment, omitting the stearic acid required 0·3 c.c. HCl.

(5) 0.100 gramme stearic acid in very small fragments agitated with 25 c.c. water, and 3 c.c. ammonia water (10 per cent.) were extracted with the several portions of alkaloidal solvent as in an assay; the residue obtained dissolved in 8 c.c. alcohol and diluted with 30 c.c. water required after addition of 3 drops indicator and 0.5 c.c. diluted ammonia water (same as used in (3) and (4)) 0·25 c.c. HCl. In this last experiment, as in assays proper, only a small portion of the stearic acid used was extracted by the alkaloidal solvent.

These experiments prove that the influence exerted by the stearic acid does not exceed 0·05 c.c. of the HCl used in these assays corresponding to about 0·005 per cent. alkaloid on the basis of 20 grammes leaves, or about 0·01 per cent. on the basis of 10 grammes leaves; the interference is so slight that no correction was made in any assay in which stearic acid was used.

While stearic acid has not been tried in the assay of other drugs, there is no doubt but that it will prove quite successful in case the alkaloids can be titrated with hæmatoxylin as the indicator.

The results of the preceding work are given in tabular form (Table No. I), from which it will be seen that all assays were made in duplicate; where calculations involve such assays the average was used. Comparing the yield of alkaloids in the extracts with the calculated yield based upon the assay of the leaves and the yield of extract, it will be seen that the former exceeds the latter by from 20 to 33 per cent.; whilst the assay of the plasters ran a trifle higher than the calculated amount based upon the assay of the extract.

To ascertain the cause of the discrepancy between the theoretical and found percentages of alkaloid in the extract a series of assays were made with a purchased sample of powdered belladonna leaves manipulating as described, but changing the quantities of drug, solvent and water as shown in the following arrangement:

	a	*b*	*c**	*d**	*e*
Belladonna leaves	20 gm.	10 gm.	10 gm.	20 gm.	20 gm.
Ether	100 "	100 "	100 "	100 "	60 "
Chloroform	25 "	25 "	25 "	25 "	15 "
Ammonia water (10 p. c.)	10 c.c.	10 c.c.	5 c.c.	10 c.c.	10 c.c.
Water	40 "	20 "	15 "	30 "	10 "
Time of maceration	4 hrs.	4 hrs.	2 hrs.	2 hrs.	2 hrs.
Alkaloid found	0·414 p.c.	0·468 p.c.	0·418 p.c.	0·383 p.c.	0·399 p.c.

* A fifth portion of ether-chloroform of 20 c.c. used to ascertain if the extraction was complete; the residue from this extraction failed to cause an alkaline reaction with the indicator.

These results are very discordant and indicate that the time allowed for maceration (it should be recalled that the original process required but a half hour's maceration) and the quantity of aqueous solution compared with the quantity of alkaloidal solvent are important factors in the yield of alkaloid. This last factor being realized, and it is remembered that the first operation in the assay is practically the same as the third operation (removing the alkaloid from ammoniacal solution by the alkaloidal solvent), we can see where error is likely to be introduced. In the first operation it is *assumed* that the ether-chloroform used contains all of the alkaloid and that the aqueous solution is simply used to moisten and agglutinate the drug into lumps so as to assist separation of the alkaloidal solution; in the third operation three portions of solvent are used to complete the extraction of the alkaloid. It would be a parallel case if in the third operation a larger quantity of solvent were used and an aliquot portion of this taken to complete the assay. To prove what is stated, 20 grammes of the leaves were percolated with 300 c.c. alcohol (95 per cent.) in a manner to be described later (page 116), the percolate evaporated at a temperature not exceeding 50° C. and the extract obtained assayed, as previously described.

The drug exhausted by 95 per cent. alcohol was next percolated in the same manner with 200 c.c. of a menstruum, consisting of alcohol 2 volumes, and water 1 volume; the percolate was evaporated and assayed as stated above. Finally, the drug exhausted with the

diluted alcohol was percolated with 100 c.c. distilled water and treated as above. The results were as follows:

	95 p.c. Alcohol.	Dil. Alcohol.	Water.	Total.
Extract	13·40 p.c.	14·45 p.c.	8·95 p.c.	36·80 p.c.
Alkaloid	0·391 "	0·064 "	none	0·455 "

The total yield of alkaloid obtained in this experiment was exceeded only by (*b*) of the preceding series; this experiment also gives an idea of the difficulty of extracting belladonna leaves with 95 per cent. alcohol.

To determine to what extent the 20 c.c. of diluted ammonia used in the assay of the extract retained alkaloid, two portions of 20 grammes each were percolated, as described on page 116, with 300 c.c. of a menstruum, consisting of 2 volumes alcohol and 1 volume water and the *entire* quantity of extract taken for the assay (method page 116).

	Extract.	Alkaloid.
A.	26·3 per cent.	0·4839 per cent.
B.	27·7 " "	0·4891 " "

The results indicate that the assays of the extracts as previously made are a little low, and corroborate the statements made as to the results attending the taking of an aliquot portion.

Another possible source of error, due to the solubility of the ether-chloroform in the aqueous solution and of water in the ether-chloroform, causing alteration in weight and volume of the alkaloidal solution, has not been separately considered. It therefore became necessary to again assay the three varieties of leaves and also the extracts prepared from them; moisture determinations were also made in the leaves, but not in the case of the extracts, as these had been placed in well-closed containers as soon as possible after their manufacture, and for these assays portions were taken from the center of the mass.

ASSAY PROCESS FOR BELLADONNA LEAVES AND EXTRACT.

Moisture.—Determined in about 2 grammes at 100° C.

Assay proper.—A small, slightly conical percolator about 8 inches long and 1¼–1½ inches wide, such as are used in certain continuous extraction apparatus, is connected with a piece of rubber tubing (about 12 inches long) having a small piece of glass tubing (about 2 inches long) attached, for the purpose of regulating the dropping of the percolate; this can also be regulated by use of a brass spring.

Into this percolator is first introduced a plug of cotton of such size as to practically fill up the neck of the percolator; place 20 grammes of the powdered leaves in the percolator, add 50 c.c. menstruum (alcohol 2 volumes, water 1 volume) and stir with a heavy iron wire until a homogeneous mixture results and in such a manner that the air-bubbles are brought as completely as possible to the surface; rinse the wire and sides of the percolator with 25 c.c. of the menstruum and allow to macerate for 5–6 hours or over night. Percolation is then allowed to slowly proceed until about 75° C. percolate are obtained when the percolation is stopped for a 5–6 hours' maceration; percolation and maceration alternate each other until 300 c.c. menstruum have been used; by evaporating the percolate in a weighed porcelain dish (about 150 c.c. capacity) until the extract could be no longer stirred with a glass rod, the yield of extract was obtained.

From this point on the assay of the leaves and of belladonna extract are identical; the extract in the dish obtained from the 20 grammes leaves (or about 5 grammes belladonna extract weighed into a beaker) are disintegrated by using 10 c.c. acidulated water (2 c.c. H_2SO_4, U.S.P., to make 500 c.c.) and stirring with a glass rod; when accomplished the mixture is transferred to a separatory funnel and the vessels rinsed with several small portions of acidulated water of 2 c.c. each; then dissolve and remove to the separator chlorophyll and other substances insoluble in the acid water by using three portions of 10 c.c. each of a mixture of ether-chloroform (ether 4 parts and chloroform 1 part by weight); now rinse the vessels (dish or beaker) with sufficient acidulated water to make the total quantity of this 25 c.c., adding this to the liquids in the separator, and finally add 20 c.c. more of the ether-chloroform. Agitate thoroughly and, after separation of the liquids, allow the acid solution to run into a beaker; repeat with 15, 10 and 5 c.c. acidulated water. Collect the first three portions together, reserving the last portion to rinse the beaker containing the first portions; clean the separator, introduce the acid solutions, finally rinsing the beaker with 5 c.c. water, add 25 c.c. ether-chloroform (ether 2 parts, chloroform 4 parts by weight; this mixture was found preferable in those extractions in which stearic acid was necessary to break up emulsions) and agitate thoroughly; after separation transfer the ether-chloroform solution to a smaller separator (about 100 c.c. capacity) and repeat

the extraction with 15, 10 and 5 c.c. of the solvent; while this last portion is separating, run the other portions through a small filter into a clean, dry flask of about 120 c.c. capacity; rinse the smaller separator with the last extraction and transfer to the filter; the stem of the larger separator is rinsed with 5 c.c. of the solvent and this portion used to again rinse the smaller separator before transferring to the filter; now rinse the stem of the smaller separator with a few cubic centimetres of the solvent, allowing this portion to run on the filter, and wash the filter and funnel with several small portions of solvent. Any aqueous solution transferred to the smaller separator should be prevented from getting on the filter and the latter should be covered as much as possible to prevent evaporation of the solvent. Should an emulsion form at any stage of the extraction of the alkaline solution, add a small fragment of stearic acid and manipulate as described on page 112.

Distil off the solvent on a water-bath, warm until the odor of chloroform disappears, dissolve the residue in 5 c.c. ether, evaporate, redissolve residue in 5 c.c. ether, evaporate and heat until the odor of ether disappears; dissolve in 8 c.c. neutral alcohol, add 30 c.c. water and 3 drops hæmatoxylin solution and titrate with standardized HCl to the disappearance of any red shade or the formation of a pure yellow color.

In this assay process in which so much inert matter is present, it frequently happens and particularly in the absence of stearic acid that a pulverulent yellow precipitate separates from the alkaline solution and must be transferred to the smaller separator and from there to the filter, where it impedes filtration.

The alkaloidal residue generally has a light greenish color, but this, as a rule, does not interfere with the end reaction in the titration; in only two out of fourteen assays was there any difficulty in the titration.

It is unnecessary to make more than the following comments upon this assay process: it is not a quick process; it has for its object the complete extraction of the alkaloids from a definite weight of the drug or preparation; one of its most important uses will be the determination of the value of any shorter assay process.

The results on page 120 were obtained by this assay process:

TABLE No. I.

Variety of Belladonna Leaves.	Leaves for Assay.		Leaves for Extract.		Extract.				Plaster.		
	Moisture. (1)	Alkaloid Found. (2)	Moisture. (3)	Alkaloid Calc. from (1), (2) and (3). (4)	Yield (5)	Moisture. (6)	Alkaloid Found. (7)	Alkaloid Calc. from (4) and (5). (8)	Loss in Making. (9)	Alkaloid Found. (10)	Alkaloid Calc. from (7) and (9). (11)
	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.
English Cultivated, Allen's	9·05	*a* 0·410 *b* 0·409 Average 0·4095	9·55	0·4072	30·488	16·04	*a* 1·7647 *b* 1·7680 Average 1·76635	1·3356	1·05	*a* 0·3576 *b* 0·3576	0·570
German Cultivated	9·15	*a* 0·396 *b* 0·392 Average 0·394	9·23	0·3936	32·20	17·24	*a* 1·5004 *b* 1·4705 Average 1·48545	1·2223	1·07	*a* 0·305 *b* 0·305	0·3003
German Wild	9·43	*a* 0·316 *b* 0·321 Average 0·3185	9·98	0·3165	26·514	15·35	*a* 1·585 *b* 1·533 Average 1·559	1·1937	0·94	*a* 0·3156 *b* 0·3156	0·3147

TABLE No. II.

Variety of Belladonna Leaves.	Leaves for Assay.		Leaves for Extract.		Extract				Plaster.		
	Moisture. (1)	Alkaloid Found. (2)	Moisture. (3)	Alkaloid Calc. from (1), (2) and (3). (4)	Yield. (5)	Moisture. (6)	Alkaloid Found. (7)	Alkaloid Calc. from (4) and (5). (8)	Loss in Making. (9)	Alkaloid Found. (10)	Alkaloid Calc. from (7) and (9). (11)
	Per Cent.	Per Cent	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.
English Cultivated, Allen's .	5·40	[a] 0·5996 b 0·6040 Average 0·6023	9·55	0·5947	30·488	16·04	a 1·851 [b] 1·828 Average 1.8395	1·950	1·05	[a] 0·3576 [b] 0·3576	0·371
German Cultivated	7·60	[a] 0·5155 b 0·5050 Average 0·5103	9·23	0·5013	32·20	17·24	[a] 1·598 [b] 1·585 Average 1·592	1·5568	1·07	[a] 0·305 [b] 0·305	0·3218
German Wild	6·80	[a] 0·4997 [b] 0·4997 Average 0·4997	9·98	0·4816	26 514	15·35	a 1·6998 [b] 1·7133 Average 1 7065	1·8164	0·94	[a] 0·3156 [b] 0·3156	0·3445

[a] Stearic acid used.

	Leaves.			Extract.
	Moisture. Per Cent.	Extract. Per Cent.	Alkaloid. Per Cent.	Alkaloid Per Cent.
English, cultivated (Allen's) .	8·40	*a.* 33·55	*a.* 0·5996	*a.* 1·8510
		b. 32·55	*b.* 0.6054	*b.* 1·8280
German, cultivated	7·60	*a.* 36·55	*a.* 0·5155	*a.* 1·5980
		b. 36·30	*b.* 0·5050	*b.* 1·5850
German, wild	6·80	*a.* 27·00	*a.* 0·4997	*a.* 1·6998
		b. 27·45	*b.* 0·4997	*b.* 1·7133

In Table No. II we have these results substituted for the corresponding ones of Table No. I. A comparison of these two tables shows a most notable increase in the assay of the leaves by the finally adopted method which removes the discrepancy shown in (7) and (8) of Table No. I.

In the assay of the extracts the final method shows slightly higher results, averaging about 0·1 per cent. alkaloid ; this makes the calculated percentage of alkaloids in the plaster a little higher than that found, a result naturally to be expected.

The yield of extract obtained from the leaves, 26·5 to 32·2 per cent., is much higher than the yield usually published, 20 to 24 per cent.; this is no doubt due to the use of more menstruum, about 6 volumes having been used for 1 part by weight of the drug; in those cases in which the extract obtained in the assay of leaves was weighed, there was used about 15 volumes menstruum for 1 part by weight of the drug, and it will be noted that the percentage of extract was increased (see top of page). By comparing the percentage of alkaloid calculated for the extract from the assay of the leaves and that found in the extract the possibility of incomplete extraction of the alkaloid is indicated in the cases of the English cultivated and the German wild leaves.

A study of the results of Table I indicates that it is possible, in assaying leaves by a process giving low results and assaying an extract by a process which very closely indicates the true alkaloidal percentage of the same, to obtain figures which apparently confirm total extraction of the leaves with a yield of say about 20 per cent. extract.

An investigation is now wanted having for its object the determination of the quantity of menstruum needed for the extraction of belladonna leaves with assays of the preparations, so that the relation between yield of extract and alkaloidal percentage can be ascertained.

SYRUP OF HYDRIODIC ACID.

By F. W. Haussmann.

Research Committee E, Pharmacopœia Revision.

Few official preparations have been subjected to as much adverse criticism as this syrup.

The objections are based chiefly on chemical grounds, and suggestions to omit it from the Pharmacopœia or to recommend recent preparations from a solution of hydriodic acid have frequently been published in various journals.

In view of the popularity enjoyed in many localities, acquiescence to such demands would be ill-timed and unjust, and the policy of condemning a preparation because changes take place which with due precaution may in a measure be prevented, or, after taking place, remedied with but little difficulty or cost, with no impairment of appearance or diminution in strength, would prove only beneficial to manufacturers.

A result of its omission from the Pharmacopœia would be the liability of physicians to specify private makes. Under the pretence of superior stability such preparations would displace the official article, while such claims are in no manner either substantiated or justified.

Syrup of hydriodic acid, prepared according to official directions, is equal to any similar preparation in the market, may be confidently recommended as such, and the material decrease in cost by self-manufacture should induce every pharmacist to prepare his own syrup.

PREPARATION.

The Pharmacopœia directs the hydriodic acid for the syrup to be prepared by double decomposition between potassium iodide and tartaric acid, preventing the liberation of free iodine by the addition of potassium hypophosphite.

Diluted alcohol is employed to prevent solution of the precipitated potassium bitartrate.

The writer has no substitute to offer in preference to this method.

The formula of the Pharmacopœia of 1880, which directed the acid to be prepared by the action of hydrogen sulphide upon an alcoholic solution of iodine, was deservedly unpopular, and the pre-

ference universally given to the present process is in the main due to its ready manipulation.

The Pharmacopœia, in furnishing its working formulas, must primarily consider the ease with which they are manipulated.

Difficult processes are seldom if ever attempted by the average retail pharmacist, and are as a rule profitable to manufacturers.

Preparations should also be directed to be made from compounds easily obtainable, in active use and as inexpensive as possible.

Chemicals, which are not used for any purpose but as ingredients in a preparation, should not be ordered, if they can be replaced by those more frequently employed.

These thoughts occurred to the writer, while manipulating various formulas for this preparation.

Syrup of hydriodic acid, as prepared by the official process, will contain a small quantity of potassium bitartrate.

The insignificant amount present is unobjectionable, but with the view of avoiding the same, the writer prepared hydriodic acid by double decomposition between barium iodide and sulphuric acid, but foreseeing the objection to the limited use of the barium salt, this process was abandoned.

For this and other reasons it must be deemed advisable to retain the present official process.

But in several particulars it is open to improvement.

The amounts of potassium iodide and tartaric acid may first be considered.

The Pharmacopœia orders 13 grammes of the former and 12 grammes of the acid to be used in preparing 1,000 grammes of the syrup.

These quantities, in the writer's experience, are insufficient to furnish a 1 per cent. syrup.

In an examination of a number of specimens of the syrup, prepared strictly according to official directions, the writer found the same to fall short of the official requirement, when estimated with decinormal silver nitrate V. S.

This is due to the fact, that the official quantities of potassium iodide and tartaric acid are calculated too close.

To demonstrate this point, the following calculation, first with potassium iodide, must be employed:

$$KI + H_2C_4H_4O_6 = HI + KHC_4H_4O_6$$
$$165{\cdot}56 \qquad\qquad 127{\cdot}53$$

As 1,000 grammes of the syrup contain 10 grammes of hydriodic acid, the following proportion gives the amount of potassium iodide required for this quantity:

$$165{\cdot}56 : 127{\cdot}53 :: x : 10.$$

$x = 12{\cdot}98$, this quantity being calculated as absolute potassium iodide.

This salt, as found in commerce is never absolute, and the Pharmacopœia allows impurities to the amount of 0·5 per cent.

If to the above calculated figure (12·98) we add this percentage, the amount of iodide necessary must be $12{\cdot}98 + {\cdot}065 = 13{\cdot}045$ grammes, a quantity already in excess of the one directed by the Pharmacopœia.

Few commercial iodides, however, show this percentage.

A similar condition also exists in the case of tartaric acid. The calculation, upon which the official quantity is evidently based, may be expressed as follows:

$$KI + H_2C_4H_4O_6 = HI + KHC_4H_4O_6$$
$$149.64 \qquad 127{\cdot}53$$
$$149{\cdot}64 : 127{\cdot}53 :: x : 10.$$

$x = 11{\cdot}73$, the amount calculated to decompose exactly 12·98 grammes of absolute potassium iodide.

It may be questioned if the potassium hypophosphite employed in the process, exists as salt or as hypophosphorous acid.

The hypothesis that the latter is the case, is probably correct.

Some authors who have experimented with the syrup, recommend an addition of hypophosphorous acid to that already present in the syrup.

To completely decompose both potassium iodide and hypophosphite, the amount of tartaric acid directed by the Pharmacopœia is insufficient.

For the decomposition of the hypophosphite by means of tartaric acid we have the following equation:

$$KPH_2O_2 + H_2C_4H_4O_6 = HPH_2O_2 + KHC_4H_4O_6$$
$$103\,91 \qquad 149\,64$$
$$103{\cdot}91 : 149{\cdot}64 : 1 : x.$$

$x = 1{\cdot}44$ grammes of tartaric acid required to decompose 1 gramme of potassium hypophosphite.

From the above figures the deduction must be made, that, to obtain a 1 per cent. syrup of hydriodic acid, the quantities of potassium iodide and tartaric acid must be increased.

The following table records an examination of specimens of syrup of hydriodic acid obtained from various sources:

EXAMINATION OF COMMERCIAL SPECIMENS OF SYRUP OF HYDRIODIC ACID BY RESIDUAL TITRATION WITH $\frac{N}{10}$ KSCN SOLUTION.

Color.	Number of c.c. $\frac{N}{10}$ $AgNO_3$ Solution consumed to precipitate 12·753 grammes of syrup.	Percentage of HI.	Remarks.
1. Brown	9·4 c.c.	·94	
2. Straw	8·7	·87	
3. Slightly straw . .	9·0	·9	contains glycerin
4. Brown	9·1	·91	
5. Amber	7·8	·78	
6. Colorless	10·1	·101	
7. Brownish	6·5	·65	
8. Colorless	10·9	·109	contains glycerin
9. Amber	9·2	·92	
10. Straw	8·4	·84	grape sugar deposit
11. Yellowish	7·6	·76	
12. Colorless	9·0	·9	U.S.P. syrup
13. Yellow	9·2	·92	heavy deposit in syrup
14. Colorless	10·2	1·02	sp. gr. 1·318
15. Colorless	10·1	1·01	sp. gr. 1·318

The process directed of washing the precipitated potassium bitartrate with diluted alcohol directs attention to another point, namely, the wasteful method of removing the hydriodic acid.

If the directions of washing the precipitate until the filtrate gives a slight precipitate when dropped into silver nitrate T. S., are followed, it will be found that considerable diluted alcohol is necessary, and a doubt is also left in the mind of the operator.

Several conditions furnish the reason.

In using the official quantities of potassium iodide and tartaric acid, a thorough washing is necessary to even approximately furnish a syrup of the required strength.

The removal of the hydriodic acid is not as easily accomplished

as supposed, the writer having found in one instance that over 150 c.c. of diluted alcohol were required in preparing 1,000 grammes of the syrup, until application of starch paste and chlorine water showed its complete removal.

If the present quantities and directions are to be retained, this reaction should be substituted for the silver nitrate test, as being more delicate and a better identity test.

Potassium bitartrate is slightly soluble in diluted alcohol and also precipitates silver nitrate T. S.

Should this direction be retained, the reading should be as follows: Until a drop or two, allowed to fall into silver nitrate T. S., produces but a slight precipitate, *almost* completely soluble on the addition of nitric acid.

Acting on the necessity of an increase in the quantities of potassium iodide and tartaric acid, a number of trials were made.

If the iodide is increased to 13·5 grammes and the acid to 12·5 grammes, the latter, however, being still insufficient to decompose all the hypophosphite with formation of the corresponding acid, a syrup can be prepared which contains 1 per cent. or over of hydriodic acid.

The washing of the precipitated potassium bitartrate until the acid is completely removed will be unnecessary, filtration to a definite volume removing a sufficient quantity to fulfill the official requirement.

Evaporation of the filtrate can also be dispensed with, the small percentage of alcohol not interfering with the stability of the syrup.

The syrup of the Pharmacopœia of 1880 contained 8 per cent. of alcohol, and the presence of less than 4 per cent. ought not be objectionable.

If evaporation of the hydriodic acid filtrate is avoided, the suggestion to dissolve the sugar directly in the properly diluted acid solution may perhaps be considered.

The increase in time necessary for solution will outweigh the trouble and loss occasioned by the present process of evaporation to a definite weight.

The following formula, based on the experiments described, has been found to yield a satisfactory syrup, answering to the official requirements:

Syrupus Acidi Hydriodici,
Syrup of hydriodic acid.

A syrupy liquid, containing about 1 per cent. by weight of absolute hydriodic acid (HI, 127·53), or about 1·3 grammes in 100 c.c.

	Grammes.
Potassium iodide, thirteen and one-half grammes	13·5
Potassium hypophosphite, one gramme	1·
Tartaric acid, twelve and one-half grammes	12·5
Sugar, 625 grammes	625·
Diluted alcohol	
Water, of each a sufficient quantity to make 1,000 grammes	1,000

Dissolve the two potassium salts in 15 c.c. of water, and the tartaric acid in 25 c.c. of diluted alcohol.

Mix the two solutions in a vial, shake it thoroughly and place it in ice water for half an hour, occasionally shaking. Filter the mixture through a small, rapidly-acting white filter into a bottle graduated to 75 c.c. Carefully allow the liquid to drain and wash the bottle in which the mixture was prepared and the filter repeatedly with small portions of diluted alcohol, allowing each portion to drain separately. When the desired amount of filtrate is obtained, dilute it with 275 c.c. of water, add the sugar and dissolve it by agitation without heat. Finally add a sufficient quantity of water to make the product weigh 1,000 grammes.

Strain if necessary.

If it would be deemed advisable to simply dilute the acid solution with syrup, such directions can be substituted for the more tedious method of dissolving the sugar by agitation. The specific gravity of the syrup, prepared by the latter method, closely approximates that of simple syrup, about 1·315 to 1·320.

PRESERVATION.

The Pharmacopœia gives no specific directions for preservation of the syrup.

Due to this fact it is often exposed to all light and temperature conditions.

In a previous paper the writer dwelt upon the discoloration occurring in this and other acid syrups.

The influence of summer heat was specifically mentioned to be of material importance in the production of this change.

The Pharmacopœia should give the following directions for preserving the syrup.

Syrup of hydriodic acid should be kept in well-stoppered bottles in a cool and dark place.

Some authors recommend the addition of glycerin to the syrup, with the object of preventing discoloration.

One writer recommends complete substitution of glycerin for syrup.

Glycerin will, however, not prevent the syrup from becoming discolored, as shown in numbers of specimens prepared by the writer.

Other acid syrups, to which glycerin is added to insure greater stability, will show similar changes.

The addition of glycerin to syrup of hydriodic acid gives rise to another objectionable feature, which, if found true, will absolutely exclude its use.

Hydriodic acid readily forms substitution products with organic hydroxyl compounds with formation of the corresponding iodide. From the triatomic alcohol glycerin ($C_3H_5(OH)_3$), allyl iodide (C_3H_5I) is produced by the action of concentrated hydriodic acid. If a glycerin substitute for the official syrup is prepared, it will be found that a peculiar leek-like odor is developed. Syrups in which a partial glycerin substitution is made show a like result, which in the case of syrups prepared with sugar alone was never observed.

To further investigate this point would form an interesting subject for research.

The peculiar odor described, noticeable only in syrups of hydriodic acid containing glycerin, make the presence of allyl iodide extremely probable.

The action of hydriodic acid upon alcohols may also be used as the basis for objection to the presence of ethylic alcohol in the syrup, as, under similar conditions, ethyl iodide may perhaps be formed.

No physical evidence of such a presence is, however, found either in diluted alcoholic solutions of the acid, standing for about one year or in specimens of the syrup, containing a small alcoholic percentage.

With the object of preventing discoloration some authors suggest recent preparations by diluting a concentrated solution of hydriodic acid with simple syrup.

A 10 per cent. acid solution is recommended, and a commercial article.

Experiments conducted by the writer show that solutions of hydriodic acid, in the presence of hypophosphorous acid, keep almost indefinitely without liberating iodine.

A disadvantage to be considered is the liability of discoloration

of the syrup taking place in the hands of the patient. Retail pharmacists are well acquainted with the popular suspicions in such instances.

DESCRIPTION.

The descriptive features, as presented by the Pharmacopœia, are open to criticism as well as improvement.

The official description is as follows: A transparent, colorless or not more than pale straw colored liquid, odorless and having a sweet, acidulous taste.

After stating the identity test with starch paste and chlorine water, the following is demanded: Not more than a faint bluish tint should be produced in the syrup by starch T. S. alone (limit of free iodine).

In a number of examinations of colored specimens the writer found free iodine in no instance.

The discoloration may be artificially produced by heating the syrup, and a perfectly colorless specimen may thus be turned reddish brown in ten to fifteen minutes, with no evidence of free iodine on cooling.

The statement that colored syrups of hydriodic acid may be restored by heating is not substantiated. On the contrary, they turn still darker.

Colored syrups do not lose their effect and determinations show that the percentage of hydriodic acid remains constant. A number of examinations revealed the fact that syrups, both at the time of preparation and after discoloration, show identical percentages.

RESTORATION.

Of considerable importance to the pharmacist is the restoration of the discolored syrup to its original condition.

This may be accomplished by means of animal charcoal, as pointed out by Mr. O. A. Rouillon.

Purified animal charcoal must be employed, as commercial bone-black contains phosphates, which dissolve in the acid.

To determine if animal charcoal also has the power of absorbing hydriodic acid, a number of specimens of the syrup were examined as to their acid percentage before and after decolorization.

In all cases no loss of acid was found, and restoration of the discolored syrup by these means is perfectly legitimate.

The proportion of animal charcoal is directed by Mr. D. Cameron to be ½ ounce of animal charcoal to the pint of syrup.

In the writer's experience the amount necessary is dependent upon the degree of discoloration, very dark syrups requiring greater amounts.

The following process has been found to give satisfactory results:

Mix the discolored syrup with from 3 to 5 per cent. its weight of powdered purified animal charcoal in a bottle, allow to stand from two to three hours with frequent agitation and filter.

Should the filtrate not be perfectly colorless, an additional amount of charcoal must be used.

PERCENTAGE ESTIMATION.

The Pharmacopœia gives the following directions for valuation:

If 32 (31·88) grammes of the syrup be exactly neutralized by ammonia water and then mixed with two drops of potassium chromate T. S., it should require about 25 c.c. of decinormal silver nitrate V. S. to produce a permanent red tint (corresponding to about 1 per cent. of absolute hydriodic acid). Extreme care must be used in neutralizing the syrup with ammonia water.

Theoretically calculated, only ·425 grammes of the official aqua ammoniæ are required to exactly neutralize the stated quantity.

The end of the reaction depends upon the formation of red silver chromate.

Errors may be made either in the case of incomplete neutralization or trifling excess of ammonia.

Silver chromate is soluble both in diluted nitric acid and ammonia water.

In the case of incomplete neutralization, addition of silver nitrate V. S., while precipitating silver iodide, will cause a corresponding amount of nitric acid to be liberated, which redissolves the silver chromate formed with destruction of the red color.

An excess of ammonia water produces allied results and errors amounting to several cubic centimetres of the $\frac{N}{10}$ silver nitrate V. S. may result therefrom.

A slight error may also take place by the presence of potassium bitartrate in the syrup.

As a substitute for the chromate titration, residual titration of $\frac{N}{10}$ silver nitrate V. S. with decinormal potassium sulpho-cyanate V. S. in the presence of nitric acid and ferric ammonium sulphate T. S. may be employed.

The advantages of this process are the following:

(1) Smaller amounts of the syrup and decinormal silver nitrate V. S. are required for the operation.

(2) The liability of error, as incurred in the neutralization with ammonia water, is diminished.

(3) The presence of potassium bitartrate does not interfere with an accurate estimation.

(4) The process is manipulated more rapidly.

Comparison with the chromate titration show the results to agree closely.

The following process, based upon the official method for the valuation of syrup of iodide of iron, may therefore be substituted for the present official method:

If 12·76 grammes (12·753 grammes) of the syrup and 15 c.c. of water be introduced into a flask and the liquid mixed successively with 11 c.c. of decinormal silver nitrate V. S. and 5 c.c. each of diluted nitric acid and ferric ammonium sulphate T. S., it should not require more than 1 c.c. of decinormal potassium sulpho-cyanate V. S. to produce a reddish-brown tint, which persists after shaking (corresponding to at least 1 per cent. of hydriodic acid).

THE ANALYSIS OF COMMERCIAL VERATRINE.

PART I.

By George B. Frankforter and Levi B. Pease.

The study of the alkaloids of the various species of *veratrum* began in 1819, when Pelletier and Caventou[1] obtained from the seed of *Veratrum sabadilla*, a substance which possessed remarkable alkaloidal properties. This substance they called "Veratria," and it was known and sold under that name in pharmacy. A very similar substance was obtained a year later from *Veratrum album*. Experiments showed later, however, that the so-called "veratria" was a mixture of several alkaloids and methods for their separation

[1] *Ann. Chim. et de Phys.* (II), 14, 69.

were subsequently given. One of these substances, perhaps the most abundant, was called veratrine. Unfortunately, these latter experiments, resulting in the isolation of these new bases, only led to confusion, for not until recently was it possible to obtain samples of the same name, with the same physiological and chemical properties. This confusion was largely due to the fact that several different substances were known under the name of veratrine. The introduction of the so-called "Merck Veratrine" has changed matters to some extent, although samples of this base have been found to vary considerably, and samples from the different factories were found to vary widely.

One of the chief causes of this variation is the extreme difficulty with which these alkaloids crystallize, thus excluding one of the most important means of purification. Another, and the chief cause, is due to the fact that several of these substances have been known by the common name veratrine.

Couerbe,[2] in his work on the separation of the alkaloids in "veratria," isolated three distinct substances, two of which were carefully studied. The most important one he called veratrine, and gave to it the formula,

$$C_{34}H_{43}N_2O_6.$$

Merck,[3] in an examination of the substances obtained by Couerbe, found that when one of these substances was dissolved in dilute alcohol and allowed to evaporate slowly, a crystalline substance was obtained, to which he gave the formula,

$$C_{32}H_{52}N_2O_8.$$

This was likewise called veratrine.

Wiegelin,[4] in a study of Veratrum album, isolated two other alkaloids besides veratrine, to which he gave the formula,

$$C_{52}H_{36}N_2O_{15}.$$

Wright and Luff[5] examined the crude alkaloid, and likewise isolated three distinct bases, giving to the substance which they called veratrine, the formula,

---

[2] *Ann. Chim. et de Phys.* (II), **52**, 367.
[3] *Ann. d. Chem. und Pharm.*, **95**, 200.
[4] *N. Jahrb. Pharm.*, **37**, 94.
[5] *Jour. Chem. Soc.*, London, **33**, 338.

$$C_{37}H_{49}NO_9,$$

and to a second, which was obtained by a method not unlike that used by Couerbe for the separation of sabadilleine, they gave the name cevadine. To this substance, they gave the formula,

$$C_{32}H_{49}NO_9,$$

Later experiments showed that cevadine was the most abundant of the three bases. It retained the name from the fact that it formed cevadic acid.

In as much as recent experiments have shown cevadine to be identical with the common veratrine, it would appear that no less than three distinct substances have been known as veratrine, any one of which might be taken as official veratrine. A number of examinations of commercial veratrine were made, and in each case the predominant base was the cevadine, so carefully described by Wright and Ahrens. Not a single case showed more than a small per cent. of either of the other substances known as veratrine.

SUBSTANCE INSOLUBLE IN ETHER.

In making these determinations, all of the different samples which could be obtained were examined. While the variation, in certain cases was considerable, the greater part was found to be the so-called Wright cevadine. The melting-point was found to vary slightly, although the general physical and chemical properties were comparatively uniform. In determining the solubility, however, it was found that when treated with ether, a small quantity of undissolved substance remained, the major part forming a colorless solution. This insoluble substance was filtered off and examined. It was an amorphous powder in each case, with a melting-point of 184° to 285° C. It did not fully answer the description of either of the above mentioned bases. The following determinations give the respective per cents. of the insoluble substance with their respective melting-points:

Name of the Manufacturer.	Merck.	Tromsdorff.	Powers & Weightman.	Mahlenkrodt.
Insoluble substance	0·86	3·89	3·6	3·26
Melting-point	184°	285°	206°	231°

It is evident, from the wide range of melting-points, that the insoluble substances from these different samples varies widely. They are at present under examination.

The soluble parts, both from melting point and from analyses, were found to be identical with Wright cevadine. The following is a comparison of melting-points and analyses:

Calculated for $C_{32}H_{49}NO_9$.	Merck. No. 1.	Merck. No. 2.	Tromsdorff.	Powers & Weightman.	Mahlenkrodt.
C = 64·96	64.6	64·5	64·72	64·74	64·82
H = 8·29	8·4	8·6	8·36	8·19	8·41
Melting-point	148°		147°	148°	148°

The above samples were of recent preparation. Two samples which had been prepared some years ago, were on examination found to resemble the "veratria" of Caventou, and were, as hitherto found, a mixture of several substances.

From the above analyses, it is evident that the principal part of veratrine in the market at the present time is identical with the substance formerly known as cevadine. In fact, the physical and chemical properties correspond exactly with those given by Wright for cevadine. While there is little doubt that the cevadine of Wright is identical with the so-called "Merck veratrine" and the veratrine of the other firms above mentioned, some of the true cevadine has been obtained and is now in comparison with the common veratrine.

PROXIMATE ANALYSIS OF THE LEAVES OF LIATRIS ODORATISSIMA.

By Charles Falkenhainer.

Contribution from the Chemical Laboratory of the Philadelphia College of Pharmacy. No. 181.

Liatris odoratissima, Michx. is a plant which grows in southern United States. It is commonly called deer's tongue, southern vanilla and vanilla plant. These names were probably suggested by certain characters of the leaves of the plant. The radical leaves are obovate-spatulate, obtuse, about seven-veined, narrowed below; the stem leaves are oval or oblong and clasping at the base. All the leaves are rather fleshy, pale green, and smooth, and after drying have a very agreeable odor, which is likened to that of the vanilla bean. This odor is due to coumarin as was pointed out by Prof. William Procter, Jr., in the American Journal of Pharmacy, 1859, page 557.

The odorous principle is present in considerable quantity, and is frequently noticeable in crystals upon the surface of the leaves.

The leaves are said to be very largely employed in the southern part of the United States to flavor tobacco, and to preserve wearing apparel from moths. Their agreeable and persistent odor renders deer's-tongue leaves also serviceable in the preparation of sachet powder and other articles of perfumery, as suggested by Dr. A. W. Miller in this JOURNAL, 1875, page 116.

The parts of the plant seem to have never been systematically analyzed. For the purposes of this study of the proximate composition of the leaves, a portion of the finely-ground material was exhausted with solvents in the succession in which their extracts are hereinafter described. The percentages given are based on the air-dried, powdered leaves.

Petroleum Ether Extract.—This extract, as obtained by spontaneous evaporation of the solvent at the room temperature and subsequent drying over sulphuric acid, amounted to 3·25 per cent. of the leaves. It exhibited a distinctly, crystalline principle. When dried to a constant weight at 110°, the extract lost weight to the extent of 0·3 per cent. of the leaves. There appeared to be a loss of crystalline principle during this treatment. The extract consisted of fatty substances soluble in hot absolute alcohol, and a wax which was also soluble in hot absolute alcohol, but redeposited on cooling. This wax was also soluble in chloroform and carbon disulphide, but insoluble in glacial acetic acid and cold alcohol. The crystalline principle previously referred to remained dissolved in the alcohol upon the cooling of the solution from which the wax deposited. It was afterwards separated from the accompanying fats by recrystallization from cold alcohol. This principle proved to be coumarin and will be subsequently treated of in this paper.

Ether Extract.—The leaves were next treated with official ether, which extracted 4·26 per cent. of their weight of a brownish-black, amorphous mass. This extract was treated with hot water, which dissolved very little substance, but acquired an acid reaction.

The aqueous solution so obtained gave reactions as follows:

Ferric chloride, greenish color.

Lead acetate, no visible change.

Fehling's solution suffered no reduction.

Fehling's solution suffered no reduction after the aqueous solution had been boiled with acid.

Another portion of the said aqueous solution was agitated with ether. This solvent, upon separation and evaporation, left a crystalline residue. This eventually proved to be coumarin.

That part of the ether extract which was insoluble in hot water, was soluble both in hot alcohol and acetone. The alcoholic solution gave a black precipitate with alcoholic solution of ferric chloride, and a green precipitate with alcoholic solution of lead acetate. When a third portion of the alcoholic solution was poured into water a precipitation of the dissolved substances took place. Besides the coumarin and the resinous matters indicated by the last three tests, the ether extract contained some wax.

Absolute Alcohol Extract.—This extract amounted to 5·74 per cent. of the leaves. It was treated with hot water, which dissolved everything, but a little chlorophyll. The aqueous solution had a very slightly acid reaction. Fehling's solution applied to it, failed to show the presence of glucose, but after boiling the aqueous solution with acid, this reagent was reduced to an extent indicating 0·43 per cent. of cane sugar. The aqueous solution produced a green color with ferric chloride. The extract contained no inorganic matter.

Water Extract.—The organic solids of the cold water extract of the leaves represented 42·96 per cent. of their weight. Alcohol added to the solution of the water extract in the proportion of five volumes of the former to one of the latter precipitated 17·28 per cent. of mucilage and albuminous matters. 4·75 per cent. of glucose was indicated in this extract; cane sugar was absent. Tannin too was absent, as was also shown by tests applied to a cold water infusion of a fresh portion of the leaves.

Alkaline Water Extract.—When the residue of the leaves from the treatments with the foregoing solvents was treated with water made distinctly alkaline with sodium hydrate, 8·44 per cent. of organic extract was removed. This amount included 2 per cent. of mucilaginous matter, which was precipitated when the solution was acidified with acetic acid, and then mixed with five times its volume of alcohol.

Acidulated Water Extract.—Water acidulated with hydrochloric acid was next applied to the residue of the leaves. This solvent dissolved 2·59 per cent. of organic matter. Not more than traces of the dissolved substances were precipitated by making the solu-

tion alkaline with ammonium hydrate, or by mixing the alkaline liquid so obtained with several volumes of alcohol.

Starch was not found in the material examined.

A portion of the powdered leaves lost 6·1 per cent. of its weight upon complete drying at 110°. This loss in the presence of the coumarin must be taken as indicating only approximately the moisture in the air-dried leaves.

The residue from drying left upon ignition 8·75 per cent. of ash. About 70 per cent. of this ash was soluble in water. The water solution had an alkaline reaction, and contained sodium, potassium, sulphur trioxide and chlorine. The remainder of the ash, with the exception of a trace of silica, dissolved in hydrochloric acid with effervescence, showing carbonates. The hydrochloric acid solution contained calcium, magnesium, aluminum and phosphoric oxide.

Coumarin.—As already stated, Professor Procter pointed out the presence of coumarin in this plant. As he did this from the observation of certain chemical behaviors which he found the substance to possess, it was thought desirable, in this connection, to make an elementary analysis of the substance with the view of adding to his results. For this purpose a quantity of the ground material was extracted with petroleum ether, the solvent removed by evaporation at ordinary temperature, and the crystalline matter of the residue repeatedly recrystallized from hot alcohol until the melting-point of the crystals was constant. The constant point was found to be between 66° and 67° C. This purified material was submitted to elementary analysis, with the following result:

	Per Cent.	Calculated for Coumarin.
Carbon	75·00	73·97
Hydrogen	4·72	4·12
Oxygen	20·28	21·91

The accepted formula for vanillin, to the odor of which that of the plant is likened, indicates carbon, 63·15, hydrogen, 5·34, and oxygen, 31·51 per cent.

It may not be out of place here to say that the melting-point of coumarin, as given by different authors, is the same, as illustrated by the following examples, taken from Husemann and Hilger's "Pflanzenstoffe:" According to Zwenger and Bodenbender, it melts at 64° C.; according to Perkin, at 67° to 67·5° C.; according to

Buchner, at 50° C.; while Kossman found it to melt at 40° C.; but in the last case the melting-point was very likely lowered by the substance being contaminated with fat.

LITHIUM CITRATE.

By Lyman F. Kebler.

Research Committee E, Pharmacopœia Revision.

This is the most important lithium salt, excepting the carbonate, now in use. It is used quite extensively and has been the subject of several investigations. But there seems to be considerable difference of opinion as to whether the hydrous[1] or the anhydrous salt is the proper article. The U.S.P. recognizes the anhydrous, while the 1898 Br.P. recognizes the hydrous. If it is the aim of the Pharmacopœias to recognize that article which is of a constant composition, the choice lies with the crystalline product. It has been shown a number[2] of times that the product containing the full quota of water of crystallization is uniform in composition, while the so-called anhydrous, may contain from 1 to 4 molecules of water of crystallization. It is anything but uniform.

In order to get more information along this line the writer collected samples from various parts of the United States and made some of the crystalline product on both the large and small scale.

The results are collected in the table on next page:

[1] Hydrous, as here used, means the salt with 4 molecules of water of crystallization.

[2] 1875, J. Umney, "Year-Book of Pharm.," 559.

1883, C. Thompson, *Pharm. Jour. and Trans.*; Am. Jour. Pharm., 55, 314.

Number.	Physical Appearance.	Microscopical Appearance.	[1] Soluble in Water at 15° C.	Per Cent. of Moisture Lost at 100° C., in 6 hours.	Per Cent. of Moisture Lost at 110° C., in 6 hours.	Per Cent. of Moisture Lost at 115° C., in 8 hours.	Per Cent. of Moisture Lost at 115° C. to 120° C.	Per Cent. of Moisture Lost at 140° C., in 8 hours.	Per Cent of Lithium Citrate.
1 . .	Crystals.	Crystals.	1 in 2·42	10·00	14·36	16·51	16·51	21·13	98·68
2 . .	Crystal powder.	Crystals.	1 in 2·43	0·00	0·40	8·34	8·34	13·19	98·73
3 . .	Powder.	Crystals and amorphous.	1 in 2·43	0·10	0·50	7·23	10·93	12·00	98·94
4 . .	Powder.	Crystals and amorphous.	1 in 2·47	19·90	20·00	22·13	22·40	24·90	99·05
5 . .	Crystal powder.	Crystals and amorphous.	1 in 2·48	16·93	19·50	21·22	23·20	25·50	98·56
6 . .	Crystal powder.	Crystals.	1 in 2·42	0·20	1·50	5·14	5·70	12·49	98·60
7 . .	Crystal powder.	Crystals and amorphous.	1 in 2·38	0·60	5·00	5·10	5·30	12·36	98·81
8 . .	Crystals.	Crystals.	1 in 2·44	17·50	20·00	22·50	23·40	25·57	98·79

[1] This is the anhydrous chemical.

There seems to be some difference of opinion as to whether or not the article is deliquescent. Before a judgment can be passed, it must, first of all, be decided whether the hydrous or the anhydrous product is meant. The 1898 Br.P. says the hydrous salt is deliquescent. The writer has exposed powdered lithium citrate, containing the full quota (25·5 per cent.) of water of crystallization to an atmosphere saturated with moisture (raining more or less all the time) for three days, and there was not a sign of deliquescence. He has also seen a container of a similar article exposed for months and the only sign of deliquescence was a slight lumpiness, which could hardly be attributed to any such cause.

On exposing the samples, dried to a constant weight at 140° C., to a saturated atmosphere, as above, six deliquesced very rapidly and the other two only slowly. Enough, however, to call them deliquescent in a moist atmosphere. The conclusion would be that the hydrous product is not deliquescent, while the perfectly dry article is more or less deliquescent. It should be noted, however,

that after the samples had taken up a certain amount of moisture, they became brittle and non-deliquescent.

Those which possessed the highest per cent. of water of crystallization appeared to be the most deliquescent, after having been dried as above. That these dried products possessed considerable avidity for water was manifested from the rise of temperature, developed when the dried articles were added to water, or *vice versa*.

Just why the various makes of lithium citrate, dried side by side, behaved so differently, when exposed to the atmosphere is difficult to say. They were all of the same degree of fineness.

The degree of solubility is another factor that depends on the kind of salt considered. The anhydrous salt, according to W. A. Puckner,[1] is soluble in 2·38 parts of water at 15° C. The results obtained in this investigation indicate that lithium citrate is somewhat less soluble, on the average, than this; or one part of lithium citrate requires 2·434 parts of water at 15° C. The solubility of the hydrous article, based on the results obtained for the anhydrous, is one in 1·91 parts of water at 15° C. This is exactly what was obtained by experiment. The solubility as given by the British Pharmacopœia, for this article, is about correct, viz.: that it is entirely soluble in twice its weight of cold water.

The anhydrous lithium citrate is soluble in about one-fourth its weight of boiling water. This is equivalent to the water of crystallization of the hydrous product. On taking the melting-point of the salt containing four molecules of water of crystallization, in a capillary tube, it became pasty at 100° C., and at 115° C. a perfect solution was obtained. The boiling-point of a saturated solution of the anhydrous article varied from 115° C. to 120° C. Neither the hydrous nor the anhydrous salts are soluble, to any appreciable extent, in either alcohol or ether.

The aqueous solutions were either neutral to litmus or slightly acid.

On ignition there is left a blackish residue, consisting of a mixture of carbon, lithium carbonate and the oxides of lithium.

In estimating the amount of water of crystallization some unexpected results were obtained.

After drying some of the products at 115° C. for eight hours, then estimating the amount of pure lithium citrate, it was surprising

[1] 1892, *The American Druggist*, page 65.

to find that the results were considerably below what they should have been theoretically. Several samples were then dried at 140° C. and in every case an additional amount of moisture was lost corresponding to differences indicated by the analytical results. Then the moistures of all the samples were carefully taken, and the results obtained are recorded above. They were all dried in the air-bath at the same time.

The above results were obtained from the same material dried at the above temperatures, from six to eight hours. The amount of water lost at 100° C. corresponded, approximately, to three molecules of water of crystallization, when four molecules were present.

Not all of the water seems to have been lost by drying at from 115° C. to 120° C. for eight hours. This would indicate that a higher temperature than the above, is required to completely dissipate the water. It may be that a lower temperature than 140° C. will suffice to produce an anhydrous article, but the above temperature is safe, and the chemical does not seem to be injured.

A 5 per cent. solution, acidulated with acetic acid, should not be affected by hydrogen sulphide, ammonium oxalate, or sodium cobaltic nitrite; neither should ammonium sulphide produce more than a faint coloration, or silver nitrate or barium chloride more than a faint opalescence, when added to the above solution.

The U.S.P. method for eliminating an excess of other alkalies is the best obtainable for the present for this salt.

The directions given for estimating the amount of pure lithium citrate in this chemical, have not given the writer satisfactory results. For comments on this operation see this JOURNAL, Vol. 71, page 61. Unfortunately, the ammonium sulphate process is not applicable. There is such an abundance of intumescence that the ammonium sulphate does not act well, and the incineration becomes very tedious.

The following method gives good results: Weigh about 0·5 gramme of the anhydrous, powdered salt into a platinum capsule; porcelain will answer; to this add, in drops from a pipette, so as to get as complete a mixture as possible, about 1 c.c. of concentrated sulphuric acid. Place the mixture on a water bath a few minutes, so that the sulphuric acid will thoroughly permeate all of the lithium citrate. Now incinerate. Apply the flame gradually at first, to avoid spirting. If the work has been well done, the lithium citrate has been completely converted into the sulphate.

One gramme of the anhydrous salt yields 0·7861 of a gramme of lithium sulphate, or the amount of lithium sulphate multiplied by 1·272 gives the equivalent of lithium citrate.

The average of the above results is somewhat below the present pharmacopœial requirement. This may be due to a possible loss during incineration, for it was noticed that when a flame was held above the capsule during the first portion of the operation, a crimson coloration was imparted to it. This is also the case with the ammonium sulphate process, and simple ignition of any organic lithium salt. As is well known, a very minute quantity of lithium imparts a crimson color to the flame. The gases evolved in the first portion of the operation apparently carry off enough of the lithium compounds to produce this coloration. Whether the amount evolved is weighable or not has yet to be determined.

35 Poplar Street, Philadelphia.

EXAMINATION OF SOME OFFICIAL FLUID ACIDS.

Contribution from the Chemical Laboratory of the Philadelphia College of Pharmacy. No. 181.

The purity and strength of medicine is always a matter of interest to both the physician and pharmacist. For this reason, it has been the custom in the Chemical Laboratory, during several years past, to have students examine samples of official medicines dispensed by pharmacists, in order to ascertain how closely these agree with the pharmacopœial requirements of purity and strength.

The samples referred to in the present contribution were purchased from wholesale and retail druggists in Philadelphia. In each case, the official article was asked for. The results of the examinations serve to indicate the variations in quality to which such simple and inexpensive medicines are liable, while the knowledge of such variations from the official standards emphasizes the necessity of the retail pharmacist testing his purchases and products in order that he may supply the public with medicines of uniform purity and strength.

Josiah C. Peacock,
Director.

Acidum Aceticum.—Robert T. Berry, P.D., examined twelve samples of acetic acid. All of the samples corresponded to the

pharmacopœial description—"a clear, colorless liquid, having a strong vinegar-like odor, a purely acid taste, and a strongly acid reaction." All of them, however, left some residue upon evaporation. None of the samples contained copper, lead or other poisonous metals. Samples 1, 9 and 12 were free from both hydrochloric and sulphuric acids; samples 3, 8, 10 and 11 contained traces of sulphuric acid; the other samples were contaminated with both of these impurities. Only samples 6 and 8 responded to the test for formic and sulphurous acids. Sample 11 was the only one which exceeded the limit of empyreumatic substances allowed by the Pharmacopœia. The samples contained the following percentages of absolute acetic acid: 36·9, 44·0, 37·2, 44·9, 45·0, 31·5, 44·8, 44·7, 44·8, 40·6, 50·6, and 45·2. The official strength is 36 per cent.

Acidum Hydrobromicum Dilutum.—David K. Bishop, P.D., titrated ten samples of diluted hydrobromic acid according to the directions of the Pharmacopœia. By this means he found the strengths of the samples to range as follows: 10·6, 10·4, 10·9, 12·0, 10·1, 13·9, 14·3, 15·0, 14·1, 12·3 per cent. The Pharmacopœia requires the presence of 10 per cent. of real hydrobromic acid.

Acidum Hydrochloricum Dilutum.—Swain H. Brewton, P.D., estimated the absolute hydrochloric acid contained in ten samples of diluted hydrochloric acid. The following percentage amounts were found: 10·85, 11·00, 10·09, 3·70, 10·20, 10·30, 11·12, 8·68, 9·37 and 11·40. To be official the preparation must contain 10 per cent. of absolute hydrochloric acid.

Acidum Hydrocyanicum Dilutum.—Claude R. Middleton, P.D., considered this subject. The Pharmacopœia requires diluted hydrocyanic acid to contain 2 per cent. of absolute hydrocyanic acid. Pharmacists are directed by the same authority to keep the substance in small, dark amber-colored, cork-stoppered vials, in a cool place. But, notwithstanding this direction, the five different samples of the acid procured were contained in glass-stoppered vials, and only one of these vials was of amber-colored glass. The samples were carefully estimated, using for each estimation five times the quantity specified by the Pharmacopœia, so as to reduce the error of titration. The respective samples showed 1·30, 1·73, 2·80, 1·69 and 1·40 per cent. of absolute hydrocyanic acid. All were colorless and all except No. 5 evaporated completely; it left a trace of residue.

Acidum Hypophosphorosum Dilutum.—Ralph L. Haus, P.D., found the physical properties of the five samples of diluted hypophosphorous acid sold to him to correspond to the description given by the Pharmacopœia. The total acidity of each sample calculated as hypophosphorous acid was first determined according to the official method. By this process the samples showed 16·0, 11·0, 16·1, 10·1 and 14·5 per cent., respectively. They were then titrated with potassium permanganate volumetric solution as further directed by the Pharmacopœia. The corresponding results by this method were 15, 10, 16, 9 and 14 per cent., showing the presence of foreign acids in the samples. The Pharmacopœia requires *about* 10 per cent. of absolute hypophosphorous acid; the allowable variation implied by the word *about* being 2 per cent. of the 10 per cent. of hypophosphorous acid, either way.

Acidum Lacticum.—William R. Bready, Jr., P.D., examined four samples of lactic acid of different makes. The first sample contained chlorides, sugars and glycerin. It showed 73·9 per cent. of absolute lactic acid. The second sample showed traces of chlorides, sulphates and sugars; it assayed 74·8 per cent. of absolute lactic acid. Samples 3 and 4 contained sugars only. Both of these were found to represent 75 per cent. of lactic acid. All of the samples were free from sarcolactic acid, iron and lead.

Acidum Phosphoricum Dilutum.—Theodore S. Schlauch, P.D., investigated twelve samples of this substance. All the samples except No. 1 were colorless and odorless; it had a milky white color and a disagreeable odor. Samples 1, 8 and 9 contained sulphates. Sample 1 alone showed chlorides, phosphates and heavy metals. All were free from nitric and phosphorous acids. The percentages of phosphoric acid present were: 10·5, 11·0, 10·0, 16·5, 10·9, 5·0, 10·0, 19 5, 24·0, 22·5, 8·5 and 7·3.

Acidum Sulphuricum.—Ernest A. Troth, P.D., procured samples of the sulphuric acid put upon the market by seven different manufacturers, and sold as the official article. Samples 1, 3 and 7 were entirely free from impurities. Samples 2 and 6 contained a small amount of nitrous acid and a large amount of hydrochloric acid. Sample 4 held an appreciable amount of lead sulphate in solution. Sample 5 showed a considerable amount of hydrochloric acid. All were free from arsenic, copper and iron. The amounts of absolute sulphuric acid calculated from the total acidities of the several samples were: 79·39, 94·03, 96·68, 91·99, 97·43, 97·38 and 98·06 per

cent. It will be seen from these figures that but two of the samples contained less than the 92·5 per cent. of absolute sulphuric acid required by the Pharmacopœia.

Acidum Sulphuricum Aromaticum.—Charles W. Beyerle, P.D., made an examination of twelve samples of this preparation for the purpose of estimating the amount of official (92·5 per cent.) sulphuric acid present in them. The results indicated 10·26, 15·33, 12·20, 11·34, 10·26, 13·39, 12·42, 16·41, 11·34, 11·34, 10·80 and 9·72 per cent. The Pharmacopœia requires the preparation to contain *about* 20 per cent. of the official sulphuric acid, the variation thus allowed being between 19·6 and 20·4 per cent.

Acidum Sulphurosum.—John E. Coleman, P.D., examined eight samples of sulphurous acid. All the samples were clear and colorless. Sample 8 was odorless; the odor of sample 3 was very faint. All showed sulphuric acid, and failed to evaporate without leaving a residue. The official method of estimating the sulphur dioxide was applied to the samples with the following results: 3·4, 3·45, 0·007, 2·49, 4·3, 1·5, 0·175 and 0·002 per cent. These results show a great variation from the official requirement of 6·4 per cent. of sulphur dioxide.

A COMMON ERROR IN RECORDED RESULTS OF PROXIMATE PLANT ANALYSIS.

By Lyman F. Kebler.

Under the above title the writer made a few remarks which appeared in the January number of this Journal. From a certain portion, it might appear that the schemes of analysis were being criticised, and the editor justly appended a foot-note, in this connection. The impression thus conveyed is, however, incorrect. It was clearly stated at the outset, that the remarks were in reference "to an error frequently made in recording the results of proximate plant analysis." The last sentence of the first paragraph imparts the wrong idea. Line *seven*, from the top of this paragraph, should read, "they are frequently recorded again," instead of, "they must necessarily be recorded." The error referred to is not due to the analytical schemes, but to inadvertent recapitulations. Any one can ascertain this for himself, by consulting the literature of proximate plant analysis during the past fifteen years. It will be found that the ash is doubly recorded, either in part or as a whole, again and again.

RECENT LITERATURE RELATING TO PHARMACY.

DIGITALIS LEAVES.

Pharmaceutische Rundschau (1898, 603) prints an extract from the "Bericht" of the firm of Cæsar and Loretz, concerning digitalis. It states that the crop of 1898 up to August 1st, contained a higher percentage of digitoxin than that of the same period of 1897; while the August harvest was poorer than that of 1897. Cultivated plants —even those originally wild—yielded less digitoxin than the wild, and the drug picked in August was weaker than that collected in June. The drug from non-flowering plants contains more dixitoxin than that collected at the same time from plants in bloom.

The digitoxin strength is lessened by exposure of the powder to air and sunlight.

Both digitalis root and seed contain digitoxin—the latter 0·162 per cent.

Pure digitoxin is insoluble in water, yet, from infusion of digitalis, considerable quantities of the principle is obtainable. In explanation, it is said that the drug contains other glucosides, forming digitoxin on digestion. H. V. ARNY.

QUANTITATIVE ESTIMATION OF CAFFEINE AND THEOBROMINE.

W. Kunz (*Schw. Wochensch. für Chem. und Pharm.*, 1898, 301) submits a method of assay of the two alkaloids, which he states gives good results. The outlines of the process are: extraction of drug with boiling water; removal of gum, etc., from infusion by freshly precipitated lead hydrate; filtration; removal of lead from filtrate by carbonic oxide gas; evaporation of filtrate to dryness with sand; and extraction of residue with ether. The ethereal solution, on evaporation, leaves a mixture of pure theobromine and caffeine. These are separated by precipitation and weighing of theobromine as silver salt. H. V. A.

ESTIMATION OF NICOTINE IN TOBACCO.

This assay is conducted by R. Hefelmann (*Ph. Centralh.*, 1898, 523) by treating 20 grammes of the powder with 20 c.c. of 6 per cent. solution of potassa, shaking with 200 c.c. ether and withdrawing in pipette 50 c.c. of the ethereal layer. This is evaporated in a current of air and the alkaloid extracted from the fatty residue

with 10 c.c. alcohol, the solution diluted with 50 c.c. water and titrated with $\frac{1}{10}$ normal sulphuric acid; hæmatoxylin or cochineal being used as indicator.

For more exact assay, the residue from 50 c.c. of the ethereal solution is treated with 10 c.c. water and a few drops solution of soda, and distilled with steam until 400 c.c. distillate is obtained. This is titrated as above.

In German tobacco, cigars and cigarettes advertised as free from nicotine, the author found that alkaloid in quantities ranging from 0·35 per cent. to 1·53 per cent. H. V. A.

CHILEAN SOLANUM SPECIES.

A popular remedy of Chile is "Natri," being the leaves and shoots of Solanum crispun, *Ruiz et Pavon;* S. gayanum, *Remy*, and S. tomatello, *Remy*. It is employed as infusion in measles and scarlet fever. Ramdohr and Neger (*Ph. Centralh.*, 1898, 521) extracted from it 0·1 per cent. solanin. H. V. A.

PHARMACOLOGICAL NOTES.

THYROID EXTRACT.

Samuel Bell, M.D. (*Journal American Medical Association*, November 19, 1898), in an interesting paper on "Thyroid Extract," states that, according to some very reliable authorities, two main theories have been advanced concerning the action of the thyroid gland. "The first is the auto-infection theory—the gland having for its function the destruction of the natural toxins; without the latter we have the condition known as myxedema. The second is the internal-secretion theory—the thyroid being considered as a secreting gland. The secretion is taken up by the lymph vessels, and is necessary for the proper metabolism of the body, especially for nervous and connective tissue. According to either of these theories, the administration of the desiccated gland supplies the lacking secretion, which may be some chemic substance that is necessary to health or even life. Ewald, in a pithy sentence, states that the gland acts as an antitoxin against certain elements that appear as by-products of tissue change. The exact constituents of this substance have never been definitely made known. An organic

iodin compound from the sheep thyroid has been extracted, called thyro-iodin, and in the present state of our knowledge the weight of authority is in favor of this being the effective chemic agent in thyroid therapy." J. L. D. M.

POISONING BY CANNABIS INDICA—RECOVERY.

Saxby (*British Medical Journal*, October 15, 1898) reports a case of poisoning from two teaspoonfuls of tincture of Cannabis indica. The patient was perfectly well at 9.15 o'clock. At 10 o'clock his pulse was weak and irregular, and the heart-sounds faint. The whole body was bathed in perspiration and cold, the limbs flaccid and the plantar reflex absent. The pupils were widely dilated, contracting slightly when a candle was placed near the eye. The patient could not be roused, and the conjunctival reflex was absent. The injection hypodermically of gr. $\frac{1}{50}$ of strychnine sulphate was followed by prompt response. The patient opened his eyes, understood what was said to him, but was unable, at first, to speak. He was given gr. $\frac{1}{10}$ of apomorphine hypodermically, after which he vomited promptly and profusely, and he then recovered rapidly.—*Phila. Med. Jour.*, p. 946. J. L. D. M.

EDITORIAL.

IMMUNITY OF CERTAIN ANIMALS TO POISONS.

In an editorial in a recent issue of this JOURNAL attention was directed to the difficulty of framing a definition as to what constitutes a poison. The expression, "What is one man's meat is another man's poison," is applicable not only to man, but the whole animal as well as plant kingdom. Arsenic, while commonly believed not to be injurious to plants, is shown by the investigations of Stoklasa to be highly poisonous to some plants, in relatively minute quantities. Many experiments have been made to determine the toxicity of various substances on plants, and the results obtained would seem to indicate (as suggested by Frank) that there is a difference in certain plants to absorb toxic substances; this having been particularly verified in analyses of peas, violets, silenes, etc., growing in soil containing zinc.

In the animal kingdom it is particularly noteworthy that some animals enjoy an unusual immunity from the action of certain poisonous plants. Goats can eat the leaves and other parts of stramonium and are apparently not affected. Horses, goats and sheep can eat conium leaves with impunity. Birds may likewise eat the berries of belladonna. In an article in the *National Druggist* (1897, p. 103) the writer shows that *Cytisus repens* (Laburnum) can be eaten with impunity by ruminants of all kinds, but is deadly to horses. The hedgehog is not affected by either cantharides or the venom of vipers. The pig is likewise

well known to be immune to the poison of rattlesnake. Hyoscyamus, while it is deadly to man, monkeys, deer, rodents and birds, is harmless to horses, goats, sheep and domestic horned animals. Morphine, is harmless to goats, sheep, antelopes and other animals. These animals can tolerate as much as 2 to 2¼ grains of morphine to the pound weight of individual.

In a recent issue of the *Scientific American* is contained a letter from *Nature* in which the correspondent observed a number of thrushes feeding on the berries of *Pyrus aucuparia* and that the ground was covered with ejected seeds and skins of the fruit. He also noted that while the pulp had disappeared, the skins were as bright as ever, showing that they could not have passed through the alimentary canal. The excessive drought, by decreasing the supply of their ordinary food, was evidently the cause of the birds taking the berries at such an early period in September. The same correspondent observed a similar case in the fruit of the yew. Another writer observed thrushes stupefied from eating the berries of *Daphne Mezereum*, but in this case there is little question but that the seeds were ejected. Another writer found that pheasants were killed by eating the leaves of the yew tree, and similar instances are recorded. Everyone is familiar with the manner in which owls disgorge the fur and bones of mice and the skulls of small birds—a habit which is shared by all the raptorial birds. The habit of ejecting the indigestible and poisonous parts of foods by birds is an interesting subject for observation and experiment.

A few years ago a short article appeared in the *Bulletin of Pharmacy* (1891, p. 116), by Frank Nabers, on "A New Use for Strychnine." The writer states that "in certain districts of the country, especially the mountainous parts of the Southern States, farmers find it almost impossible to successfully raise poultry, on account of the depredations of hawks. When the chickens have reached that very toothsome age of 'spring,' the hawks, in spite of the vigilance of the farmers, succeed in carrying them off, to such an alarming extent, that the poor farmers, in their desperation, are willing to resort to any device which will rid them of the bold marauders. The plan which they have adopted is as follows, and a unique one it certainly is: A quantity of 'nux vomiky buttons' are procured and powdered about as fine as ordinary corn meal. A very generous supply of this unpalatable meal is added to the chickens' food, and as the chicken is a bird which digests its food entirely by mechanical means, gravel, sand, etc., it is not affected at all by the strychnine, which is practically insoluble in water (solubility being about 1–36,000) and does not act locally, but only by absorption, thus large quantities can be given the chickens with impunity, and still not interfere with their use as an article of food for man, as the strychnine remains undissolved in the entrails. But when the unsuspecting hawk takes one of these doctored fowls to his lofty home, he is seized with an attack of indigestion, or rather digestion of strychnine, after eating his stolen meal, from which he never recovers. For the hawk is a carnivorous bird, hence its digestion is a chemical one instead of mechanical, and as the entrails are to him the daintiest portion, he gets into his stomach the greater part of the undissolved drug, which is acted upon by digestive fluids present in the stomach, forming soluble compounds, which, being absorbed, result fatally."

This article interested the present Editor of the AMERICAN JOURNAL OF PHARMACY to the extent of performing some experiments a few years ago. A small chicken, weighing about three-quarters of a pound, was isolated and

fed on corn-meal containing various percentages of powdered nux vomica for several days.

On July 17th, at 8 A.M., it was given meal containing 0·18 grain of nux vomica. At 1.20 P.M. of the same day, it was again given meal containing 0·18 grain of nux vomica.

On July 18th, at 8 A.M., the chicken was given a mixture of cornmeal containing 0·36 grain of pure nux vomica. At 11 A.M., 0·72 grain was given.

On July 19th, at 8 A.M., 2 grains of nux vomica were given it with its meal. All of the meal containing the nux vomica was eaten, and it was considered that the experiments afforded some evidence that nux vomica was not toxic to the chicken. The chicken was allowed its freedom and watched for some time, and gave every evidence of being rather improved by the treatment.

This opens up a rather interesting practical problem. Cannot some of our drugs, after the extraction of medicinal constituents, be utilized as food for poultry, etc., just as linseed- and cotton-seed meals are fed to cattle? All of our roots and rhizomes, fruits and seeds are rich in food materials which can, no doubt, be utilized after the extraction of their active principles for medicinal preparations, in feeding some of the lower domestic animals. This is well worth the consideration of large manufacturing firms where thousands of tons of exhausted drugs are doubtless daily thrown away.

REVIEWS AND BIBLIOGRAPHICAL NOTICES.

OUTLINES OF INDUSTRIAL CHEMISTRY, A TEXT-BOOK FOR STUDENTS. By Frank Hall Thorp, Ph.D., Instructor in Industrial Chemistry in the Massachusetts Institute of Technology. New York: The Macmillan Co. London: Macmillan & Co., Ltd. 1898. Price, $3.50, net.

The author states that the object of this book is to furnish an elementary course in industrial chemistry, which may serve as the ground-work for a more extended course of lectures, if desired. As the whole range of chemical industries, both inorganic and organic, is covered in the compass of 528 pages, it is necessarily an outline only, and yet it can serve, satisfactorily, the purpose indicated for it by the author.

The first twenty pages are devoted to an account of the general operations necessary in most chemical industries, and we note an excellent discussion of the methods of evaporation, calling attention to the economy of fuel involved in multiple-effect systems, the Yaryan evaporator being given as illustration; under distillation, the theory of fractional condensation is clearly stated and an account given of column stills; under filtration, a description of filter presses with illustrations and the use of centrifugal machines; under refrigeration, the theory of artificial refrigerating machines, in which a volatile liquid is alternately vaporized and recondensed, is given with an illustration of the condensing and expansion vessels and the method of their connection.

Fuels both solid and gaseous are briefly but well covered.

We note with satisfaction that many new processes of importance are mentioned, processes which have not as yet been taken up in text-books generally. Thus Squibb's process for the manufacture of acetone by passing the vapors of acetic acid through heated pumice mixed with barium carbonate is

given a place. The Readman process, for the production of phosphorus by the electric furnace, which has already displaced the old distillation process in practice, is also mentioned, although the description is rather inadequate.

The section on textile industries is very satisfactorily developed, as well as those on explosives and paper-making. That on varnishes is very incomplete, and the part played by the several classes of driers is only slightly alluded to in a different section under linseed oil.

The chlorine industry is very satisfactorily treated, and the newer electrolytic processes for chlorine, hypochlorite and chlorate are also given proper attention.

A few blemishes show, and in mentioning some of them no sweeping condemnation is intended. Some of them detract appreciably, however, from the excellence of the sections in which they occur.

Thus the author states that one of the chief uses of crude sulphur is as a germicide in combating *phylloxera*, "a disease of the grape," and that this disposes of nearly one-quarter of the yearly production. The germicide used against the insect called *Phylloxera vastatrix* is either carbon disulphide or the xanthogenate of potash, made by the reaction of this latter with alcoholic potash.

The formula of bleaching powder

$$Ca\begin{cases} Cl \\ OCl \end{cases}$$

the author says was assigned by Lunge. It was first suggested many years ago by the English chemist, Odling.

Under recovered sulphur, no mention is made of Chance sulphur, which is the chief form at present produced in England.

Sodium bisulphite is given prominence as "Antichlor" in removing excess of chlorine from chlorine-bleached goods, on page 44, to the exclusion of the thiosulphate, yet in the section on paper bleaching, on page 509, the thiosulphate is referred to as the sole practical antichlor, as it is in fact.

Crude petroleum is described on page 290 as a "thick syrupy liquid." This would hardly apply to the bulk of the crude oils met with in the refineries, which is a thin greenish liquid of from 42° to 51° B.

However, these are minor matters as compared with the general excellence of the work, which, as an outline picture of our main chemical industries, is a very satisfactory piece of work.

The book has a number of helpful illustrations and lists of reference works are appended to each section. S. P. S.

PHILADELPHIA ASSOCIATION OF RETAIL DRUGGISTS.

As a result of the organization of the National Association of Retail Druggists at St. Louis, October 17, 1898, the Philadelphia Association of Retail Druggists was organized December 2, 1898, and the following officers elected:

President, Wm. McIntyre; First Vice-President, W. L. Cliffe; Second Vice-President, A. Hoch; Treasurer, Dr. Edwin R. Smiley; Secretary, W. A. Rumsey.

Executive Committee.—James C. Perry, Chairman; E. R. Gatchel, D. H. Ross, H. C. Blair, Jr., E. J. Finnerty, Jr.

At a later meeting the Constitution and By-Laws were adopted.

The question is asked by many, what does all this amount to, and what advantage will this be to me individually? A body of men working together for some general good can do more than one individual, and that is the reason almost every trade or profession have their organizations. Whatever advantage is gained by the National Association will be a benefit to each one of us, because the Wholesale Druggists' Association, and the Proprietors' Association, will hesitate to do anything which would be contrary to the wishes of the National Association, and backing the National Association there will be nearly 30,000 retail druggists throughout the United States, and it is through these druggists, that the wholesale druggist makes his money and the patent medicine manufacturer sells his remedies.

By organization a sociable feeling is created. We become more friendly one with the other, learn new ideas and improved methods of doing business, and we can unite together to promote any plan which will benefit us.

It is proposed to establish for the benefit of the members of the Association: A classified record of clerks. A credit bureau. To create a proper feeling between the physician and pharmacist, and to induce the physician to prescribe more generally the "U.S.P." and "N.F." preparations.

Our meetings are held the first Friday in each month at 3 P.M. sharp, in the museum of the Philadelphia College of Pharmacy, the use of this room having been granted to the Association by the Board of Trustees of the Philadelphia College of Pharmacy. At our June meeting delegates to the National Convention will be elected. The membership dues are one dollar a year, and the hearty co-operation is asked of all retail druggists in Philadelphia, that our Association may be a success, that we may become a power in the National Association and an honor to the profession which we represent.

W. A. RUMSEY,
Secretary, P. A. R. D.

MINUTES OF THE PHARMACEUTICAL MEETING.

PHILADELPHIA, February 21, 1899.

The regular monthly Pharmaceutical Meeting was held in the Museum of the College, with Wallace Procter in the chair.

The minutes of the previous meeting were allowed to stand as published.

As a result of the recent belladonna plaster controversy, Prof. F. X. Moerk furnished a paper on "The Assay of Belladonna Leaves, and Some of Its Preparations," which will no doubt prove to be a most important contribution to the literature of the subject (see page 105).

A paper, incorporating improved formulæ for the "Syrups of Acacia and Althæa," was presented by F. W. Haussmann, and will be published in full in a subsequent issue of this journal.

Speaking on the preservation of syrups, Wallace Procter said that he had been able to keep Jackson's Pectoral Syrup almost indefinitely by the addition of small quantities of oil of sassafras. Professor Ryan stated that almost any

syrup which was sterilized and stoppered and kept in a cool place, would keep indefinitely, this being, as he thought, one of the features of Mr. Haussmann's paper. Mr. Haussmann showed that independent of these facts the preparations made by his formula possessed greater stability than those made by the Pharmacopœial and other formulæ. Professor Ryan also alluded to the usefulness of chloroform as a preservative for the syrup and mucilage of acacia, which fact is quite generally known. Dr. Wendell Reber believed that when antiseptics were employed they should be innocuous and tasteless, as otherwise confusion was likely to arise in the mind of the patient. He also alluded to the possible use of formalin as a preservative in pharmaceutical preparations. Mr. Procter stated that he found formalin useful in keeping milk of asafœtida.

Mr. Frederick L. Lewton exhibited a collection of cardamoms, and in connection therewith made some interesting remarks, which will be referred to in a later issue of this JOURNAL.

Professor Ryan alluded to the collection in the College of seven specimens of cardamoms sent by Mr. Daniel Hanbury to the late Professor Procter. These were interesting, as they were labelled in the handwriting of Mr. Hanbury.

Dr. Wendell Reber read a paper on the "Chemistry of the Mydriatic Alkaloids." This was based on the more recent researches of Pinner, which aimed to clear up the ambiguity on the nomenclature of this class of substances. Those participating in the discussion of this paper were Mr. Kebler, Dr. Reber and the chairman.

Professor Remington exhibited one of the "Phœnix Emulsifiers," which had been presented to him by Messrs. Whitall, Tatum & Co. The apparatus is intended for the use of the retail pharmacist in the manufacture of emulsions of cod liver oil, and may be used according to either the Continental or English method. A cut of the apparatus is here presented, which conveys more than a description. A copying machine for either writing or typewriting, and known as the "Neostyle," was exhibited and recommended as useful for printing by pharmacists. Attention was called by Professor Ryan to the "Anchor Safety Stopper" poison bottle, which is the invention of Mr. Albert T. Plummer, of New York City. This consists of a glass rod suspended in the bottle by means of an asbestos cord, which is attached to the cork. This device serves as a warning, if, by mistake, a bottle containing poison is taken, in two ways, viz.: The sudden arrest of the cork and the rattling of the glass against the sides of the bottle. A convenient medicine dropper, invented by Dr. W. R. Sine, was also exhibited.

On motion, the meeting adjourned.

THOS. S. WIEGAND, *Registrar.*